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Date: 6/7/01 By: Deborah Brackney

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

Allen, *et al.*

SERIAL NO.: Not yet Assigned

FILED: Concurrently Herewith

FOR: **THERAPEUTIC LIPOSOME COMPOSITION AND METHOD OF PREPARATION**

EXAMINER: Unknown

ART UNIT: Unknown

Preliminary Amendment

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination and calculation of the filing fee in the above-identified application, please amend the above-identified application as follows.

In the Specification:

Please replace the first paragraph of the specification, which appears after the title "Therapeutic Liposome Composition and Method of Preparation", and before the subheading "Field of the Invention," with the following substitute paragraph:

--This application is a division of U.S. Application No. 09/517,224 filed March 2, 2000, now pending; which is a division of U.S. Application No. 09/138,480 filed August 21, 1998, now pending; which is a continuation-in-part of U.S. Application No. 08/949,046 filed October 10, 1997, now U.S. Patent No. 5,891,468;

which claims the priority of U.S. Provisional Application No. 60/028,269 filed October 11, 1996, now abandoned, which are all incorporated herein by reference.--

In the Claims: Cancel claims 1-20 and 33-58 and add new claims 59-83 as follows:

--59. (New) The conjugates of claim 21, wherein the targeting ligand is selected from the group consisting of water soluble vitamins, apolipoproteins, insulin, galactose, Mac-1, PECAM-1/CD31, fibronectin, osteopontin, RGD sequences of matrix proteins, HIV GP 120/41 domain peptomers, GP120 C4 domain peptomers, T cell tropic isolates, SDF-1 chemokines, Macrophage tropic isolates, anti-cell surface receptor antibodies or fragments thereof, pyridoxyl ligands, biotin, RGD peptide mimetics, YIGSRG protein, a_vB_5, IL-8, anti-E-selectin Fab.

60. (New) The conjugates of claim 59, wherein the anti-cell surface receptor antibodies or fragments thereof is selected from the group consisting of anti-HER2/neu, anti-selectin and anti-VEGF pyridoxyl.

61. (New) The conjugates of claim 59, wherein the pyridoxyl ligand is selected from the group consisting of pyridoxal, pyridoxine, pyridoxamine, pyridoxal 5'-phosphate and N-(4'-pyridoxyl)amines.

62. (New) A targeting conjugate, comprising (i) a lipid having a polar head group and a hydrophobic tail, (ii) a hydrophilic polymer having a proximal end and a distal end, said polymer attached at its proximal end to the head group of the

lipid, and (iii) a targeting ligand attached to the distal end of the polymer.

63. (New) The conjugate of claim 62, wherein the targeting ligand is an antibody or an antibody fragment.

64. (New) The conjugate of claim 63, wherein the antibody or antibody fragment is a humanized murine antibody.

65. (New) The conjugate of claim 62, wherein the targeting ligand specifically binds to an extracellular domain of a growth factor receptor.

66. (New) The conjugate of claim 65, wherein the receptors are selected from the group consisting of c-erbB-2 protein product of the HER2/neu oncogene, epidermal growth factor receptor, basic fibroblast growth factor receptor and vascular endothelial growth factor receptor.

67. (New) The conjugate of claim 62, wherein the targeting ligand binds a receptor selected from the group consisting of E-selectin receptor, L-selectin receptor, P-selectin receptor, folate receptor, CD4 receptor, CD19 receptor, αβ integrin receptors and chemokine receptors.

68. (New) The conjugate of claim 62, wherein the targeting ligand binds a receptor on a malignant B-cell or T-cell, said receptor selected from the group consisting of CD19, CD20, CD22, CD4, CD7 and CD8.

69. (New) The conjugate of claim 62, wherein the targeting ligand is selected from the group consisting of folic acid,

pyridoxal phosphate, vitamin B12, sialyl Lewis^x, transferrin, epidermal growth factor, basic fibroblast growth factor, vascular endothelial growth factor, VCAM-1, ICAM-1, PECAM-1, RGD peptides and NGR peptides.

70. (New) The conjugate of claim 62, wherein the targeting ligand is selected from the group consisting of water soluble vitamins, apolipoproteins, insulin, galactose, Mac-1, PECAM-1/CD31, fibronectin, osteopontin, RGD sequences of matrix proteins, HIV GP 120/41 domain peptomers, GP120 C4 domain peptomers, T cell tropic isolates, SDF-1 chemokines, Macrophage tropic isolates, anti-cell surface receptor antibodies or fragments thereof, pyridoxyl ligands, biotin, RGD peptide mimetics, YIGSRG protein, a_vB_5, IL-8, anti-E-selectin Fab.

71. (New) The conjugate of claim 70, wherein the anti-cell surface receptor antibodies or fragments thereof is selected from the group consisting of anti-HER2/neu, anti-selectin and anti-VEGF pyridoxyl.

72. (New) The conjugate of claim 70, wherein the pyridoxyl ligand is selected from the group consisting of pyridoxal, pyridoxine, pyridoxamine, pyridoxal 5'-phosphate and N-(4'-pyridoxyl)amines.

73. (New) A liposome composition comprising targeting conjugate comprised of (i) a lipid having a polar head group and a hydrophobic tail, (ii) a hydrophilic polymer having a proximal end and a distal end, said polymer attached at its proximal end to the head group of the lipid, and (iii) a targeting ligand attached to the distal end of the polymer.

74. (New) The composition of claim 73, wherein the targeting ligand is an antibody or an antibody fragment.

75. (New) The composition of claim 74, wherein the antibody or antibody fragment is a humanized murine antibody.

76. (New) The composition of claim 73, wherein the targeting ligand specifically binds to an extracellular domain of a growth factor receptor.

77. (New) The composition of claim 76, wherein the receptors are selected from the group consisting of c-erbB-2 protein product of the HER2/neu oncogene, epidermal growth factor receptor, basic fibroblast growth factor receptor and vascular endothelial growth factor receptor.

78. (New) The composition of claim 73, wherein the targeting ligand binds a receptor selected from the group consisting of E-selectin receptor, L-selectin receptor, P-selectin receptor, folate receptor, CD4 receptor, CD19 receptor, αβ integrin receptors and chemokine receptors.

79. (New) The composition of claim 73, wherein the targeting ligand binds a receptor on a malignant B-cell or T-cell, said receptor selected from the group consisting of CD19, CD20, CD22, CD4, CD7 and CD8.

80. (New) The composition of claim 73, wherein the targeting ligand is selected from the group consisting of folic acid, pyridoxal phosphate, vitamin B12, sialyl Lewis^{x}, transferrin, epidermal growth factor, basic fibroblast growth factor, vascular

endothelial growth factor, VCAM-1, ICAM-1, PECAM-1, RGD peptides and NGR peptides.

81. (New) The composition of claim 73, wherein the targeting ligand is selected from the group consisting of water soluble vitamins, apolipoproteins, insulin, galactose, Mac-1, PECAM-1/CD31, fibronectin, osteopontin, RGD sequences of matrix proteins, HIV GP 120/41 domain peptomers, GP120 C4 domain peptomers, T cell tropic isolates, SDF-1 chemokines, Macrophage tropic isolates, anti-cell surface receptor antibodies or fragments thereof, pyridoxyl ligands, biotin, RGD peptide mimetics, YIGSRG protein, a_vB_5, IL-8, anti-E-selectin Fab.

82. (New) The composition of claim 81, wherein the anti-cell surface receptor antibodies or fragments thereof is selected from the group consisting of anti-HER2/neu, anti-selectin and anti-VEGF pyridoxyl.

83. (New) The composition of claim 81, wherein the pyridoxyl ligand is selected from the group consisting of pyridoxal, pyridoxine, pyridoxamine, pyridoxal 5'-phosphate and N-(4'-pyridoxyl)amines.--

REMARKS

Claims 1-20 and 33-58 have been cancelled, and new claims 59-83 have been added.

Attached is a version with markings to show changes made to the first paragraph of the specification, marked up to show all the changes relative to the previous version of the paragraph, pursuant to 37 CFR §1.121(b)(iii).

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 324-0880.

Respectfully submitted,

Date: June 7, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

This application is a division of U.S. Application No. 09/517,224 filed March 2, 2000, now pending; which is a division of U.S. Application No. 09/138,480 filed August 21, 1998, now pending; which is a continuation-in-part of U.S. Application No. 08/949,046[,] filed October 10, 1997, now U.S. Patent No. 5,891,468; which claims the priority of U.S. Provisional Application No. 60/028,269[,] filed October 11, 1996, now abandoned, which are all incorporated herein by reference.